REMARKS/ARGUMENTS

I. Status of the Claims

Prior to entry of this amendment, claims 33-48 were pending in the application, with claims 38-43 withdrawn as allegedly directed to non-elected species. Upon entry of this amendment, claim 33 is amended without prejudice or disclaimer. This amendment merely addresses formal matters and makes explicit what was previously implicit. Thus, these amendments do not restrict the scope of the original claim, and the amended claim is entitled to the full scope of equivalents as the original claim. After entry of this amendment, claims 33-48 remain pending, with claims 38-43 withdrawn from examination.

II. Election/Restriction

The Examiner states on page 2 of the Office Action that claims 38-43 have been withdrawn because these claims are directed to non-elected *species*. It is further stated that upon allowance of the elected species that Applicants will be entitled to consideration of claims to additional species until all the species have been examined or a non-allowable species is found.

By withdrawing claims 38-43 from examination, Applicants note that the Examiner has limited examination to inflammatory diseases, which is the species of disease Applicants elected in response to the species election requirement. It also appears that examination may have been limited to ELC, the elected chemokine species. It is submitted that the full breadth of the claims should have been examined. MPEP 803.02 emphasizes that in Markush type claims, such as claims 33 and 35 that respectively recite a group of chemokines and CCX CKR mediated diseases, that examination must continue with respect to all species, unless prior art is identified that anticipates the claim or renders it obvious, as indicated in the following section:

> If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species

> shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration. . . .
>
> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. MPEP 803.02 (emphasis added).

In the instant Office Action, the Office did not identify any prior art that would render the claims unpatentable. Instead, all rejections were based upon 35 U.S.C. 112. In view of MPEP 803.02, it is thus submitted that examination should have continued with respect to non-elected species until all species had been examined on the merits or until prior art with respect to one of the species was found. Applicants thus request the Examiner to continue examination in accordance with these provisions before issuing a further communication.

III. Objections to the Specification

The sections of the specification that contain embedded hyperlinks have been amended to remove the hyperlinks as requested.

The reference to Figure 4A in the Brief Description of the Drawings and elsewhere in the specification has been amended as requested.

IV. Claim Objections

Claims 33-37 and 47-48 are objected to because they are said to recite to non-elected species. As discussed above in section II, however, it is submitted that examination should have continued with respect to these non-elected species since the Office has not yet identified any prior art that render the claims unpatentable.

The Office Action states that claim 33 should refer to "treating a CCX CKR-mediated disease" rather than "treating an CCX-mediated disease" to be grammatically correct. The claim has been amended as requested.

IV. Claim Rejections under 35 U.S.C. 112, First Paragraph

A. Enablement Rejection

Claims 33-37 and 44-48 are rejected under 35 U.S.C. 112, first paragraph as encompassing subject matter that is not enabled by the disclosure in the specification. To support this conclusion, the Office Action identifies four primary issues that are said not to be adequately discussed in the specification: 1) the appropriate dosage of the agent and how long it should be administered, 2) agents that modulate the binding of a ligand to CCX CKR, 3) diseases that are specifically associated with CCX CKR, and 4) mechanism of action of the administered agent and whether the agent should promote or inhibit interaction of CCX CKR with its ligand. These concerns will be addressed in turn.

In response to the concern that the application lacks sufficient guidance regarding dosage, mode and duration of administration, Applicants direct the Examiner's attention to page 44, lines 1-13, which provides guidance on appropriate dosage of the agent. Disclosure with respect to duration and frequency of administration is provided at page 44, lines 11-13. The specification also describes a variety of modes by which agents can be administered (see, e.g., page 41, line 13 to page 43, line 30. Several references that provide additional guidance on formulations, dosages and modes of administration are cited in and incorporated into the specification (see, e.g., page 41, lines 6-12).

With respect to the second assertion that the specification does not disclose any modulators of ligand binding to CCX CKR, the Examiner is referred to page 38 which shows chemical structures for both agonists and antagonists of ligand binding to CCX CKR. In particular, two of the compounds listed on this page (compounds I and II) are antagonists of CCX CKR binding to ELC; the third compound shown (compound III) is an agonist of CCX CKR binding to ELC. So the specification does in fact provide specific chemical structures of compounds that modulate the binding of certain ligands to CCX CKR. Moreover, the specification provides extensive guidance on how additional compounds can be identified using a variety of screening assays (see, e.g., page 33, line 29 to page 38; and example 7), including assays using specific model systems (see, e.g., page 16, lines 16-24). Additionally, the specification provides guidance on a variety of different types of molecules that can be utilized

in the current methods, including antisense polynucleotides, ribozymes and antibodies (see, e.g., page 23, line 18 to page 33, line 4).

Regarding the third concern, it is submitted that the specification provides an extensive discussion of diseases that can be mediated by CCX CKR activity. Because CCX CKR is a chemokine receptor, this receptor would be expected to be involved in those diseases correlated with chemokine activity. As noted in the background section of the specification, chemokines play a key role in inflammatory responses, leukocyte trafficking , angiogenesis and other processes that involve migration or activation of cells (see, e.g., page 1, lines 18-23). The specification also identifies a number of specific diseases associated with such activities that can be treated with CCX CKR modulators (see, e.g., page 39, line 19 to page 40, line 17).

To substantiate a role for CCX CKR in such diseases, Applicants are submitting several scientific articles which discuss the role that certain chemokines, identified in the current application as ligands for CCX CKR, can play in a variety of different diseases. An article by Weninger, et al. (J. Immunol. 170:4638-4648, 2003), for instance, discusses the role that the chemokines CCL19 (ELC) and CCL21 (SLC) have in various diseases associated with T cell recruitment, including various autoimmune and inflammatory diseases, such as rheumatoid arthritis and ulcerative colitis. Studies regarding the involvement of SLC and BLC in various types of chronic inflammation are described in an article by Hjelmstrom et al. (Am. J. Pathology 156:1133-1138, 2000). A third article by Xanthou, et al. (Arthritis and Rheumatism 44:408-418, 2001) describes results implicating ELC in a particular inflammatory disease of the salivary glands. The results from these articles, which indicate a role for chemokines that are ligands for CCX CKR in a variety of disease types, are consistent with the discussion in the specification regarding the role of CCX CKR in disease (see, e.g., pages 39-40).

Finally, as for the fourth concern, Applicants disagree that the specification does not provide the requisite guidance with respect to specific conditions that are associated with CCX CKR activity and whether ligand/receptor binding should be promoted or inhibited to achieve a desired treatment outcome. As just described, the specification in fact describes a number of specific conditions that can be correlated with CCX CKR activity. Whether a specific agent is useful in treating a particular disease can be determined without undue experimentation

by testing the agent with various in vivo model systems known in the art, including, for instance, those described in the specification for various diseases (see, e.g., page 36, lines 16-24).

B. Written Description Rejection

Claims 33-37, 44-45 and 47-48 are rejected under 35 U.S.C. 112, first paragraph as not satisfying the written description requirement. The Office Action contends that the skilled artisan cannot envision the infinite number of agents encompassed by the current claims and that conception cannot be achieved until there is reduction to practice. It is thus concluded that the written description requirement in this case is not satisfied unless the structure of the agent is presented.

In response, it is first noted that the specification does in fact provide several structures of molecules that inhibit or promote binding between CCX CKR and a ligand. To reiterate the point made above, page 38, for instance, shows two CCX CKR antagonists and one agonist.

Second, as the Office Action indicates, an inquiry underlying the written description requirement is whether the applicant has conveyed with reasonable clarity that he or she was in possession of the currently claimed invention. For the reasons that follow, it is submitted that the answer to this question is "yes."

The structure of antisense molecules and triplex olig-and polynucleotides that can be utilized in certain methods, for instance, are directly based upon the nucleic acid sequence of CCX CKR, which is provided in the specification. The specification also describes which segments of CCX CKR these agents typically are designed to bind to and how many nucleotides these type of agents typically include. Based upon this disclosure and the additional guidance provided in the cited references regarding molecular design and use of such molecules in treatment (see, e.g., page 25, lines 6-9 and 21-25; and page 25, line 34 to page 26, line 3), one of skill can envision appropriate molecules.

One of ordinary skill can also envision suitable ribozymes that could be used to inhibit CCX CKR because the structure of such ribozymes also depends upon the sequence of CCX CKR, which is provided in the current application.

From the protein structure information provided in the specification for CCX CKR and the known sequences of CCX CKR ligands, those of ordinary skill could also envision suitable antibodies that would inhibit binding of CCX CKR with its cognate ligands. Once a protein antigen is available (e.g., CCX CKR, a fragment thereof, or a chemokine ligand for CCX CKR), those of ordinary skill in the art can reasonably conclude that antibodies to these antigens are in the possession of the inventor because making antibodies to a known antigen is routine in the art (see, e.g., page 29, line 21 to page 33, line 4).

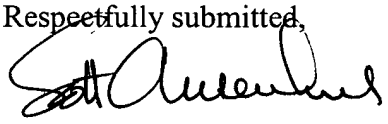
V. Claim Rejections under 35 U.S.C. 112, Second Paragraph

Claims 33-37 and 44-48 are rejected because the acronym CCX CKR is said to be vague. The acronym has been spelled out in independent claim 33 to address this concern.

These claims are also said to be indefinite because the claims lack a step that clearly relates back to the preamble. Independent claim 33 has been amended to address this concern as well.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



Scott L. Ausenhus
Reg. No. 42,271

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 303-571-4000
Fax: 415-576-0300
SLA:cmb
47104241 v1